REMARKS

Claim 14 has been canceled without prejudice. Claims 13 and 32 have been amended. Claim 39 has been added. Applicants submit that the claim amendments and new claim 39 are fully supported by Applicants' original specification and claims. The amendments are made solely to expedite prosecution of the application, and Applicants reserve the right to prosecute claims of similar or differing scope in subsequent applications. No new matter has been introduced.

Claims 17-31 are canceled as being drawn to a non-elected invention. Cancellation is made solely to expedite prosecution and Applicants reserve the right to pursue such claims in a future application.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Election/Restriction

The Examiner has acknowledged Applicants' election, with traverse, of Group I (claims 1-16) in the Response filed on July 13, 2004. Applicants note with appreciation that the Examiner has grouped newly added claims 32-38 into elected Group I.

Drawings

As the Examiner suggested, Applicants have amended the specification to refer to each Figure and to delete the reference to Figure 3D under the Brief Description of the Drawings.

Specification

Applicants have amended claim 32 to comply with the requirements for Sequence Identifiers.

Claim objections

Claim 32 is objected to under 37 CFR § 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants respectfully

disagree. According to MPEP 608.01(n)(III), "[a] dependent claim does not lack compliance with 35 U.S.C. § 112, fourth paragraph, simply because there is a question as to (1) the significance of the further limitation added by the dependent claim, or (2) whether the further limitation in fact changes the scope of the dependent claim from that of the claim from which it depends. The test for a proper dependent claim under the fourth paragraph of 35 U.S.C. § 112 is whether the dependent claim includes every limitation of the claim from which it depends."

Nevertheless, solely to expedite prosecution, Applicants have amended claim 32 by deleting the recitation "or a portion thereof" to clarify the claimed subject matter.

Claim rejections under 35 U.S.C. § 112, second paragraph

Claims 14-15 and 32-38 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

First, the Office Action asserts that claims 14-15 are vague and indefinite due to the use of the term "MuSK" as a limitation. As described above, Applicants have canceled claim 14; the subject matter of claim 14 is included in claim 13. Applicants submit that the term "MuSK" is well defined in the specification. For example, the specification teaches that "[t]he term 'MuSK' used interchangeably herein with 'muscle specific kinase,' refers to a protein tyrosine kinase, that is expressed in normal and denervated muscle, as well as other tissues including heart, spleen, ovary or retina (See Valenzuela, D., et al., 1995, *Neuron* 15: 573-584). The tyrosine kinase has alternatively been referred to as 'Dmk' for 'denervated muscle kinase.' Thus, the terms MuSK and Dmk may be used interchangeably. The protein appears to be related to the Trk family of tyrosine kinases, and is further described in U.S. Patent No. 5,814,478" (page 16, lines 14-20).

Nonetheless, in order to expedite prosecution, the term "MuSK" in claim 13 has been defined as "muscle, skeletal, receptor tyrosine kinase (MuSK)." Given the teachings of the specification and the references by incorporation, a skilled artisan would readily understand the metes and bounds of the subject matter of these claims. For example, the amino acid sequence of human MuSK can be readily identified in GenBank Accession No. NP_005583 (enclosed

herewith as **Exhibit A**). Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

Second, the Office Action objects to claim 32 for the recitation "or portion thereof." As described above, Applicants have amended claim 32 by deleting such recitation, thereby obviating the rejection.

Third, the Office Action objects to claims 33-38 as being dependent from the alleged indefinite claim (claim 32). As described above, Applicants have amended claim 32, rendering this rejection moot.

Based on the above arguments, Applicants submit that all claims as amended comply with the requirement of 35 U.S.C. § 112, second paragraph. Therefore, reconsideration and withdrawal of rejections under 35 U.S.C. § 112, second paragraph, are respectfully requested.

Claim rejections under 35 U.S.C. § 102

Claims 13-16 and 32-38 are rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Ruoslahti et al. (U.S. Patent No. 5,654,270, 1997). Applicants respectfully traverse this rejection to the extent that it is maintained in light of the amended claims.

The Ruoslahti reference allegedly discloses use of proteoglycans which include biglycan to inhibit an activity of a cell regulatory factor in scarring studies. Specifically, the Office Action alleges that "Ruoslahti et al. describe using proteoglycans in scarring studies (Example VI, columns 19 and 20), wherein decorin, a molecule homologous to biglycan (bottom at column 7 continuing to column 8), was added to a wound cut down to the skeletal musculature, thus, providing a contact with a membrane of a muscle cell . . . . one would reasonable conclude that contacting proteoglycan with a muscle cell, as described by Ruoslahti et al., lead to binding to MuSK, potentiating agrin-induced phosphorylation of MuSK and unregulated utropin levels, absent evidence to the contrary" (Office Action, page 6, lines 2-17). Applicants respectfully disagree for the reasons that follow.

To anticipate an invention, the prior art reference must disclose each and every aspect of the claimed invention. Thus, to anticipate the method of amended claim 13, a prior art reference

would have to disclose a method for activating a postsynaptic membrane of a cell, comprising contacting the cell with an effective amount of a biglycan therapeutic, wherein the biglycan therapeutic activates muscle, skeletal, receptor tyrosine kinase (MuSK) on the cell, and wherein the cell is situated in a human subject.

The Examiner alleges that the method disclosed in Ruoslahti et al. inherently possesses the elements of the claims. Applicants note that Ruoslahti et al. teach only the possible use of biglycan for reducing scar formation, and the administration of decorin in an animal model by creating a wound by cutting down to the muscle and then applying decorin. The purpose of the described experiment was to assess the effect of decorin on scar formation in a mouse. There is no teaching that cutting to the muscle would be an appropriate method for administration in a human as recited in amended claim 13, and in fact, one would presume that such a mode of administration would be highly undesirable. There is no teaching that decorin or biglycan would have any effect on muscle tissue or that there would be any situation in which it would be desirable to introduce decorin or biglycan systemically or by local injection to an unwounded tissue.

Inherency is not a matter of probabilities. As stated by the Court of Appeals for the Federal Circuit: "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). Furthermore, "In relying upon a theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

The claimed features would not necessarily flow from the method disclosed by Ruoslahti et al. Ruoslahti et al. do not state whether or not the application of decorin to an experimental incision in a mouse had any effect on MuSK in the *mouse*. Therefore, it is certainly a matter of guesswork and probability to determine whether decorin administered through an experimental incision in a *human* would have an effect on MuSK. Additionally, as noted above, the technique that Ruoslahti et al. employed in the mouse has no bearing on how one would apply the method

of Ruoslahti et al. in humans. In humans one would presumably apply decorin to a natural wound so as to prevent scarring. Such naturally occurring wounds might come in any of a host of forms, sizes and depths. Applicants assert that Ruoslahti et al. provide no evidence that administering biglycan through a naturally occurring wound in a human would achieve the presently claimed effect on a muscle cell; this is not a necessary consequence of the method. Furthermore, Ruoslahti et al. do not suggest any mode of administration in a human other than by treatment of a wound. Given that such treatment was not attempted in humans, it is not inevitable that any such treatment would result in adequate dosing to the muscle to achieve the claimed effects. Given that many, if not most, wounds would not be cut through to the muscle, Applicants assert that this mode of administration of biglycan would have a low and highly variable probability of achieving the claimed results. Furthermore, Ruoslahti et al. do not provide any motivation to one of skill in the art to modify or optimize the mode of administration of decorin or biglycan. With respect to biglycan specifically, Ruoslahti et al. only disclose that biglycan might be useful to prevent scarring in wounds. Further, Ruoslahti et al. do not describe activation of MuSK by biglycan or decorin.

Accordingly, Applicants contend that Ruoslahti et al. do not inherently disclose the features of the present claim. Nonetheless, to expedite prosecution, claim 13 is amended to specify that the cell is situated in a human. In addition, Applicants have added new claim 39 which recites a method for activating a postsynaptic membrane in a cell in vitro or ex vivo, such method comprising assaying MuSK kinase activity. Applicants submit that neither claim 13 nor claim 39 is anticipated by Ruoslahti et al.

Dependent claims 15-16 and 32-38 are not anticipated by the Ruoslahti reference for the same reasons described as above.

Based on the above arguments, Applicants submit that the cited Ruoslahti reference fails to anticipate amended claims 13, 15-16, and 32-39. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for

allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this submission, please charge the fees to our **Deposit Account No. 18-1945.** If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit account.

Respectfully Submitted,

Date: January 19, 2004

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Fax: 617-951-7050

☐ 1: NP_005583. Reports muscle, skeletal,...[gi:5031927]


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VERSION     NP_005583.1  GI:5031927
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  REMARK    GeneRIF: analysis of regulation of MuSK expression by a novel
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  AUTHORS   DeChiara,T.M., Bowen,D.C., Valenzuela,D.M., Simmons,M.V.,
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  TITLE     The receptor tyrosine kinase MuSK is required for neuromuscular
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  JOURNAL   Cell 85 (4), 501-512 (1996)
  MEDLINE   96222293
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  AUTHORS   Valenzuela,D.M., Stitt,T.N., DiStefano,P.S., Rojas,E., Mattsson,K.,
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  TITLE     Receptor tyrosine kinase specific for the skeletal muscle lineage:
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  JOURNAL   Neuron 15 (3), 573-584 (1995)
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   PUBMED   7546737
REFERENCE   4  (residues 1 to 869)
  AUTHORS   Schultz,S.J. and Nigg,E.A.
  TITLE     Identification of 21 novel human protein kinases, including 3
            members of a family related to the cell cycle regulator nimA of
            Aspergillus nidulans
  JOURNAL   Cell Growth Differ. 4 (10), 821-830 (1993)
  MEDLINE   94100173
   PUBMED   8274451
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COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final NCBI review. The reference sequence was derived from AF006464.1.

Summary: Intercellular communication is often mediated by receptors on the surface of one cell that recognize and are activated by specific protein ligands released by other cells. Members of one class of cell surface receptors, receptor tyrosine kinases (RTKs), are characterized by having a cytoplasmic domain containing intrinsic tyrosine kinase activity. This kinase activity is regulated by the binding of a cognate ligand to the extracellular portion of the receptor. DeChiara et al. (1996) [PubMed 8653786] noted that the RTKs, known to be expressed in cell type-specific fashions, play a role critical for the growth and differentiation of those cell types. For example, members of the neural-specific TRK family that recognize nerve growth factor are absolutely required for the survival and development of discrete neuronal subpopulations, and the receptor tyrosine kinases TIE1 (MIM 600222) and TIE2 (MIM 600221) play a critical role in the development of normal blood vessels.[supplied by OMIM].

FEATURES Location/Qualifiers

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